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## **Startle reactivity in the long-term after severe accidental injury: Preliminary data**

Schumacher, Sonja ; Schnyder, Ulrich ; Furrer, Michael ; Mueller-Pfeiffer, Christoph ; Wilhelm, Frank H  
; Moergeli, Hanspeter ; Oe, Misari ; Martin-Soelch, Chantal

**Abstract:** An exaggerated startle response is one of the core hyperarousal symptoms of posttraumatic stress disorder (PTSD). Heightened startle eye-blink magnitude and reduced habituation of this response in PTSD patients have been reported in several studies. However, it is unclear whether this is an enduring characteristic of individuals vulnerable for PTSD or to which degree trauma-exposed individuals who do not develop PTSD also show exaggerated startle. Thirteen accident survivors with remitted PTSD, 12 trauma controls, and 16 non-trauma controls were examined. Four measures of startle reactivity were analyzed in response to 15 bursts of white noise (95dB, 50ms): eye-blink magnitude, eye-blink onset latency, skin conductance response, and heart rate response. The eye-blink reflex was measured over the left musculus orbicularis oculi. Reactivity and habituation were analyzed using linear mixed models. Remitted PTSD subjects did not differ from non-trauma controls regarding any of the startle reactivity or habituation measures. Unexpectedly, trauma controls showed larger eye-blink magnitude than non-trauma controls. These results suggest that the exaggerated startle response disappears after remission from PTSD. Further, they suggest that psychologically resilient trauma survivors might show a PTSD-like pattern of exaggerated physiological startle even many years after a traumatic event.

DOI: <https://doi.org/10.1016/j.psychres.2013.06.034>

Posted at the Zurich Open Repository and Archive, University of Zurich

ZORA URL: <https://doi.org/10.5167/uzh-79986>

Journal Article

Accepted Version

Originally published at:

Schumacher, Sonja; Schnyder, Ulrich; Furrer, Michael; Mueller-Pfeiffer, Christoph; Wilhelm, Frank H; Moergeli, Hanspeter; Oe, Misari; Martin-Soelch, Chantal (2013). Startle reactivity in the long-term after severe accidental injury: Preliminary data. *Psychiatry Research*, 210(2):570-574.

DOI: <https://doi.org/10.1016/j.psychres.2013.06.034>

# **Startle reactivity in the long-term after severe accidental injury:**

## **Preliminary data**

Sonja Schumacher <sup>a,\*</sup>, Ulrich Schnyder <sup>a</sup>, Michael Furrer <sup>a, b</sup>, Christoph Mueller-Pfeiffer <sup>a, c, d</sup>, Frank H. Wilhelm <sup>e</sup>, Hanspeter Moergeli <sup>a</sup>, Misari Oe <sup>a, f</sup>, Chantal Martin-Soelch <sup>a, g</sup>

a) Department of Psychiatry and Psychotherapy, University Hospital Zurich, Switzerland

b) Psychiatric Hospital Königsfelden, Brugg, Switzerland

c) Center of Education and Research (COEUR), Psychiatric Services of the County of St. Gallen-North, Wil, Switzerland

d) Department of Psychiatry, Massachusetts General Hospital and Harvard Medical School, Boston, USA

e) Department of Psychology, Division of Clinical Psychology, Psychotherapy, and Health Psychology, University of Salzburg, Austria

f) Department of Neuropsychiatry, Kurume University School of Medicine, Japan

g) Department of Psychology, Division of Clinical and Health Psychology, University Fribourg, Switzerland

Location of work: Department of Psychiatry and Psychotherapy, University Hospital Zurich, Switzerland

Correspondence should be addressed to: Sonja Schumacher, Department of Psychiatry and Psychotherapy, University Hospital Zurich, Haldenbachstrasse 18, 8091 Zurich, Switzerland; Phone +41 44 255 96 41, Fax +41 44 255 44 08, E-Mail: [sonja.schumacher@usz.ch](mailto:sonja.schumacher@usz.ch)

### **Abstract**

An exaggerated startle response is one of the core hyperarousal symptoms of posttraumatic stress disorder (PTSD). Heightened startle eye-blink magnitude and reduced habituation of this response in PTSD patients have been reported in several studies. However, it is unclear whether this is an enduring characteristic of individuals vulnerable for PTSD or to which degree trauma-exposed individuals who do not develop PTSD also show exaggerated startle. Thirteen accident survivors with remitted PTSD, 12 trauma controls, and 16 non-trauma controls were examined. Four measures of startle reactivity were analyzed in response to 15 bursts of white noise (95dB, 50ms): eye-blink magnitude, eye-blink onset latency, skin conductance response, and heart rate response. The eye-blink reflex was measured over the left musculus orbicularis oculi. Reactivity and habituation were analyzed using linear mixed models. Remitted PTSD subjects did not differ from non-trauma controls regarding any of the startle reactivity or habituation measures. Unexpectedly, trauma controls showed larger eye-blink magnitude than non-trauma controls. These results suggest that the exaggerated startle response disappears after remission from PTSD. Further, they suggest that psychologically resilient trauma survivors might show a PTSD-like pattern of exaggerated physiological startle even many years after a traumatic event.

**Keywords:** startle; trauma; post-traumatic stress disorder (PTSD); psychophysiology.

### 1. Introduction

Post-traumatic stress disorder (PTSD) is an anxiety disorder that can develop after exposure to terrifying events in which grave physical harm occurred or was threatened (American Psychiatric Association, 1994). Resilience on the other hand is a personality characteristic that moderates the negative effects of stress and promotes adaptation. The rates of PTSD among accident survivors vary considerably between studies, some showing high rates of up to 46% (Blanchard et al., 1994; Blanchard et al., 1995; Ehlers et al., 1998; Koren et al., 1999; Ursano et al., 1999). In contrast, in two studies in Switzerland less than 5% of severely injured accident survivors were found to suffer from PTSD (Schnyder et al., 2001; Schnyder et al., 2008), indicating high psychological resilience in this population.

According to the DSM-IV (American Psychiatric Association, 1994), the diagnosis of PTSD includes persistent symptoms of increased arousal like exaggerated startle responses, difficulty falling or staying asleep, anger, or hypervigilance. The startle reaction is a physiologic response to a sudden unexpected stimulus that contracts several muscles in order to protect the body from harm (Landis and Hunt, 1939). Startle reactivity can be measured using the eye-blink reflex, which is part of the startle reaction and can easily be elicited by loud acoustic stimuli (Lang et al., 1990). High startle reactivity is characterized by high eye-blink amplitudes and short eye-blink onset latencies. The startle reaction can also be accompanied by a rise of the skin conductance level (Shalev et al., 1992) and an increased heart rate (Shalev et al., 1992; Orr et al., 1995; Orr et al., 1997a; Orr et al., 1997b).

Studies exploring the association between startle reactions and PTSD have found inconsistent results. In victims of single potentially traumatic events such as combat, rape, or accidents evidence for heightened startle reactions in PTSD has been found compared to traumatized subjects without PTSD (Butler et al., 1990; Shalev et al., 1992; Orr et al., 1995; Morgan et al., 1996; Shalev et al., 1997; Grillon et al., 1998) as well as compared to subjects without trauma history (Shalev et al., 1992; Morgan et al., 1996; Morgan et al., 1997; Grillon et al., 1998). Victims of prolonged or repeated traumatic exposure such as childhood sexual abuse, on the other hand, might reveal a reversed pattern of lower startle reactivity. For example Medina et al. (2001) found that higher PTSD scores were associated with lower startle reactivity in women who had experienced childhood corporal punishment or intimate partner aggression. In a meta-analysis by Pole (2007) PTSD was reliably associated with larger responses to startling sounds. It is unclear, however, whether the exaggerated

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startle response is a stable trait characteristic of subjects vulnerable for PTSD (risk factor), or an acquired PTSD symptom that disappears after remission. In accordance with the former hypothesis, in a prospective investigation Guthrie and Bryant (2005) found a heightened startle reaction in firefighters prior to trauma to be a predictor for PTSD severity after traumatic events. On the other hand, Shalev et al. (2000) found that subjects who later developed PTSD showed elevated startle responses 1 month after trauma, while 1 week after trauma they did not differ from subjects who did not go on to develop PTSD. In a rat model of PTSD Nalloor et al. (2011) showed that higher acoustic startle reactions elicited by mild stress prior to a traumatic event were able to predict PTSD-like behavior after trauma. These results suggest a hidden risk factor for PTSD that can be seen under mildly stressing conditions. Additionally, studies investigating reactions to startle sounds in PTSD reported deficits in habituation, i.e. deficits in the decrease of physiological reaction after repeated exposure (Shalev et al., 1992; Orr et al., 1995; Shalev et al., 1997). These findings point to a possible learning deficit in PTSD patients that could partly explain the hyperarousal symptoms and might have implications for treatment. Also studies investigating fear-potentiated startle reactions point into this direction by showing that the ability to inhibit fear reactions under safe conditions is impaired in PTSD patients (Jovanovic et al., 2009; Jovanovic et al., 2012).

Taken together, these findings show that the relation between startle and PTSD is rather complex. The few studies that have compared startle reactions in remitted and current PTSD patients (Metzger et al., 1999; Carson et al., 2007) also found inconsistent results. While Carson et al. (2007) found that current PTSD patients showed higher heart rate responses than remitted PTSD patients and subjects who never had PTSD, Metzger et al. (1999) found higher heart rate responses and slower skin conductance habituation in current and remitted PTSD patients as compared to individuals who never had PTSD.

Further, it is unclear how subjects who are resilient against the development of PTSD after a traumatic event react physiologically compared to individuals who have never experienced any serious traumatic event. More specifically, it is not clear whether psychologically resilient subjects show a PTSD-like pattern at the physiological level or whether physiological changes only take place in association with psychological PTSD symptoms.

The aim of this study was to investigate whether remitted PTSD subjects still show heightened startle reactions. We examined the physiological startle reactivity of accident survivors, comparing remitted PTSD subjects with a group of accident survivors who did not develop PTSD (trauma

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controls) and a group of control subjects who had not experienced any trauma (non-trauma controls). On the assumption that heightened startle might be a pre-existing trait characteristic of subjects vulnerable for the development of PTSD, we expected the remitted PTSD subjects to have the largest startle response and slowest habituation. On the other hand, we expected the trauma control group to show the weakest startle response and fastest habituation as they seem to be resilient to stress. The non-trauma control subjects were expected to lie between the other two groups, because this group should comprise both resilient and susceptible individuals.

## 2. Methods

### 2.1. Participants

Twenty-two PTSD-remitted accident survivors and 16 resilient accident survivors who had not developed PTSD were recruited from two samples of physically injured subjects who had been hospitalized at the Department of Traumatology at the University Hospital Zurich 10 years ago and had taken part in earlier studies looking into the psychosocial consequences of accidental injuries (Schnyder et al., 2001; Schnyder et al., 2008). These patients had originally received a thorough psychiatric diagnostic assessment shortly after the accident and six and 12 months later. To recruit the subjects we called all the participants of the previous studies fulfilling our inclusion criteria, and informed them about our study. Additionally, 16 healthy controls were recruited from the general population through advertisements (non-trauma group). All subjects were over 18 years of age. To be included in the PTSD-remitted group subjects had to have been diagnosed with full or subsyndromal PTSD according to DSM-IV (American Psychiatric Association, 1994), as assessed by the German version (Schnyder and Moergeli, 2002) of the Clinician-Administered PTSD Scale (CAPS) (Blake et al., 1995) at least at one of the measurement points in the previous studies (full PTSD: fulfilling symptom clusters B, C and D; subsyndromal PTSD: fulfilling symptom clusters B plus either C or D but not both) but not in the present study. For participants to be included in the trauma-control group, it was required that they never had a diagnosis of full or subsyndromal PTSD during the previous studies. Inclusion criteria for the non-trauma group were that the participants had never experienced a trauma according to DSM-IV criteria. Exclusion criteria for all three groups were current mental disorders, chronic somatic and neurological diseases and insufficient command of German. All subjects were tested for normal hearing function. Groups were matched for age and gender (see Table 1). Participants were thoroughly informed about the procedures and gave written informed

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consent according to the Declaration of Helsinki before participating. This study was approved by the local ethics committee.

Six participants were excluded from the study due to current major depression or anxiety disorders. Two participants were excluded because of non-normal hearing, and three because of technical problems. One subject canceled the assessment, and one did not tolerate the face electrodes for the startle measurement. From the remaining 13 subjects in the PTSD-remitted group, one subject was excluded from skin conductance analysis and two from heart rate analysis because of poor data quality. Also, one of the remaining 12 subjects in the trauma-control group and two of the 16 subjects in the non-trauma group were excluded from skin conductance analysis for the same reason. The sample description is given in Table 1. Two subjects in the remitted PTSD group were taking psychotropic medication, one was taking antidepressants and one anticonvulsants. Analyses were performed both including and excluding these subjects (results without these two subjects are provided in the supplemental material). Two subjects of the remitted PTSD group had received psychotherapy.

### **2.2. Psychometrics**

Current PTSD symptoms were assessed using the German version (Schnyder and Moergeli, 2002) of the Clinician-Administered PTSD Scale (CAPS) (Blake et al., 1995). Axis I comorbidity was established by the Mini International Neuropsychiatric Interview (M.I.N.I.) (Sheehan et al., 1998). Symptoms of depression were measured by the German version (Hautzinger et al., 1995) of the Beck Depression Inventory (BDI) (Beck et al., 1961) and trait anxiety by the German version of the State Trait Anxiety Inventory (STAI) (Laux et al., 1981). The absence of traumatic events in the non-trauma group was checked by the German version of the first part of the Posttraumatic Stress Diagnostic Scale (PDS) (Foa, 1995).

### **2.3. Physiological measures**

Recording of the physiological data was performed using a BIOPAC MP150 System (Biopac Systems, Inc., Goleta, CA). The eye-blink reflex was measured by electromyographic (EMG) recordings of activity in the left musculus orbicularis oculi (Fridlund and Cacioppo, 1986) using Ag/AgCl disposable snap connector electrodes filled with hydrogel jelly. Skin conductance electrodes were placed on the thenar and hypothenar eminence of the left palmar surface using Ag/AgCl electrodes filled with

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isotonic electrolyte gel. Electrocardiograms (ECG) were recorded from three Ag/AgCl disposable snap connector electrodes filled with hydrogel jelly located below the left and right collarbone and on the left rib cage. EMG and ECG were sampled at a 1000Hz rate, skin conductance level at a 62.5Hz rate.

### 2.4. Procedure

The study took place at the psychophysiological laboratory of the Department of Psychiatry and Psychotherapy, University Hospital Zurich, Switzerland. Sensors were attached while the subjects reclined in a comfortable chair. Subjects were then asked to rest quietly for 7 min in order to facilitate laboratory adaptation. Then 15 startle probes (bursts of white noise, 95dB, 50ms) were presented binaurally via Novitronic sealed headphones with variable intertrial intervals ranging from 27s to 52s. The presentation of the startle probes was done via E-Prime 2.0 Professional (Psychology Software Tools Inc., Pittsburgh, PA., USA) and a Sony STR-DE197 amplifier. Loudness was calibrated using a Voltcraft SL-100 sound-level measuring device.

### 2.5. Data reduction

Autonomic Nervous System Laboratory 2.51 (ANSLAB; Wilhelm, F. H. & Peyk, P., 2005; available at the SPR Software Repository: <http://www.sprweb.org>) was used to filter the raw data, to correct for artefacts and to extract mean and maximum scores for event and baseline windows.

The startle EMG was 50Hz notch filtered and rectified and rated for eye-blink magnitude (baseline corrected amplitude) and onset latency. The 50ms before probe onset were used as baseline. The 100ms response window started 20ms after probe onset. The onset of the eye-blink was defined as the time point when the signal reached a value higher than five standard deviations of baseline variance above the baseline mean.

The ECG signal was band-pass filtered (0.5 – 40 Hz); skin conductance level was low-pass filtered (1 Hz). Heart rate was extracted using the interval between successive R waves. Heart rate and skin conductance level were rated for a 6s event window beginning at the startle probe onset and corrected for a baseline window of 2s before startle probe onset. The baseline mean was subtracted from the event mean for the heart rate and from the event maximum for skin conductance level. For the skin conductance level a response was defined as a baseline corrected event maximum of at least 0.05  $\mu$ S. Non-responses were not included in the analysis. Skin conductance responses were log transformed ( $\ln(\text{SCR}+1)$ ) in order to normalize the distribution.



### 2.6. Data analysis

Statistical analyses were performed using PASW Statistics 18.0 (SPSS Inc., Chicago, Ill, USA). We used a linear mixed model design and applied restricted maximum likelihood estimation to analyze time effects (habituation) and to compare the three groups of subjects. Full-factorial models were built with group and time (trial) treated as fixed effects and subjects as a random effect. All models were run using all possible covariance types for the repeatedly measured outcomes. The models were optimized by the covariance type which produced the lowest Akaike's Information Criterion (AIC). A first order ante-dependent covariance structure was accommodated for eye-blink magnitude. For eye-blink onset latency the best fit was obtained with a first order auto-regressive covariance structure. For skin conductance response and heart rate response the best fit was obtained with a first order factor analytic structure. Bonferroni corrected pairwise comparisons based on the estimated marginal means were used as post-hoc tests.

### 3. Results

There was a significant main effect of group on eye-blink magnitude ( $F(2, 41.1)=3.56, P=0.04$ ). The trauma-controls showed significantly higher eye-blink magnitude ( $M=11.94, SE=2.09$ ) than the non-trauma controls ( $M=4.60, SE=1.80$ ) (mean difference = 7.33,  $SE=2.75$ , 95%-CI 0.46 to 14.21,  $P=0.03$ ). There was neither a significant difference in eye-blink magnitude between remitted PTSD subjects ( $M=8.19, SE=2.00$ ) and the trauma-controls (mean difference = -3.74,  $SE=2.89$ , 95%-CI -10.95 to 3.47,  $P=0.6$ ), nor between the remitted PTSD subjects and the non-trauma controls (mean difference = 3.59,  $SE=2.69$ , 95%-CI -3.11 to 10.30,  $P=0.6$ ). There was a significant main effect of time on eye-blink magnitude ( $F(14, 64.2)=6.49, P<0.001$ ) with magnitude decreasing over time across all groups of subjects. Skin conductance response showed a significant main effect of time ( $F(14, 91.3)=6.85, P<0.001$ ), decreasing over time across all groups of subjects. There was no significant main effect of group for skin conductance response ( $P=0.3$ ). No significant main effects were found for eye-blink onset latency and heart rate response ( $P_s>0.1$ ). No significant time by group interaction was found in any of the measures ( $P_s>0.1$ ). Figure 1 illustrates the time course of all four measures by group. Analyses without the two subjects taking antidepressants and anticonvulsants revealed the same pattern of significant effects (see supplemental material).

Descriptively, a reversal of the habituation can be seen in Figure 1 for skin conductance response in the remitted PTSD group. Pairwise comparisons showed that for the remitted PTSD group trials 6 and 8 to 11 differed from trial 1 ( $P_s\leq 0.03$ ) but trials 12 to 15 did not anymore ( $P_s=1.0$ ). For trauma controls

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only trial 11 differed significantly from trial 1 ( $P=0.05$ ) while for non-trauma controls significant differences to trial 1 could be seen for trials 8, 10, 12, 14 and 15 ( $P_s \leq 0.05$ ). Separate models for trials 1 to 6 and 7 to 15 revealed that the group effect in eye-blink magnitude only reached significance in the later part of the experiment. All other effects showed the same pattern as in the model for the whole experiment including both parts (see supplemental material). Remitted PTSD subjects and trauma controls did not differ in CAPS scores. We did not find any group differences in BDI or STAI scores, either (see Table 1).

### 4. Discussion

The aim of this exploratory study was to provide further insight into the origin of exaggerated startle responses in PTSD. We compared the startle reactivity of PTSD-remitted accident survivors with accident survivors who had not developed PTSD (trauma controls) and healthy controls who had never experienced any serious traumatic event (non-trauma controls). We found no difference between remitted PTSD subjects and non-trauma control subjects in any of the physiological measures of startle reactivity. Unexpectedly, even 10 years after the accident the trauma control group showed, in the absence of psychopathological symptoms, higher startle eye-blink magnitude than the non-trauma controls.

Our data indirectly support the hypothesis that heightened startle reactions observed in PTSD subjects (Butler et al., 1990; Shalev et al., 1992; Orr et al., 1995; Morgan et al., 1996; Morgan et al., 1997; Shalev et al., 1997; Grillon et al., 1998) might be an acquired PTSD symptom (Shalev et al., 2000) that disappears after remission. On the other hand they are not in line with the results of earlier studies suggesting the heightened startle reaction to be a trait characteristic of subjects that develop PTSD (Metzger et al., 1999; Guthrie and Bryant, 2005). A possible explanation for this discrepancy might be that we investigated a different type of trauma. Only two subjects of the remitted PTSD group had received psychotherapy, which makes it unlikely that the missing difference between the remitted PTSD group and the non-trauma controls is a therapy effect. It neither seems that psychotropic drugs are accountable for our results, as the pattern of significant effects stayed the same with and without the two subjects taking psychotropic medication.

One possible explanation for the unexpected heightened startle eye-blink magnitude we found in trauma-controls is that the experience of trauma, even if not related to psychopathological symptoms, might elicit physiological changes. This means that psychological resilience could still be associated

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with physiological symptoms of PTSD. It is unclear, however, why the heightened eye-blink magnitude had not recovered in trauma controls, despite similar traumatic events as had been experienced by the remitted PTSD subjects. It could also be speculated that dealing with and recovering from psychological problems restores normal learning functions while in people who do not develop psychological problems in the first place dysfunctional learning might persist on the physiological level. On the other hand, though not significant, our data might also indicate instable learning in skin conductance responses in remitted PTSD patients.

Important limitations of this study are its small sample size and the rather broad confidence intervals we found for mean differences, raising questions regarding the reliability of our findings. We wish to emphasize that these preliminary results do not necessarily reflect a generalizable feature for the majority of remitted PTSD patients and resilient people. Another shortcoming is that we have no information about the subjects' startle reactivity before the accident or during the PTSD episode in the remitted PTSD group. Therefore, we cannot rule out the possibility that the startle reactivity of the trauma controls differed from the non-trauma controls already before the traumatic event or that our sample of remitted PTSD subjects did not show heightened startle reactions while they suffered PTSD symptoms. A group of current PTSD patients would have allowed a direct comparison with the reactivity in symptomatic subjects but unfortunately it was not possible to recruit a comparable group from the previous studies. Furthermore, we investigated only participants that had experienced accidental physical injuries, while earlier research on trauma and startle was often performed on subjects with war-related traumatic experiences. As war and accidental injury are completely different sorts of potentially traumatic events it might well be that different processes underlie their startle reactivity. Due to these limitations these initial results in an underexplored area clearly need to be replicated. Ideally, a longitudinal design should be used to disentangle the exact time course of startle reactivity in trauma survivors over the time span of several years. It might also be informative to include a measure of subjective resilience into a longitudinal design to see how subjective attitudes change over time and if they are associated with physiological measures.

In conclusion, this study provides a first and preliminary indication of heightened startle in trauma survivors who had not developed PTSD. The fact that remitted PTSD subjects did not differ from non-trauma controls indirectly supports the idea of heightened startle reactions being a symptom of PTSD rather than a trait of individuals who develop PTSD. The difference between trauma survivors who had not developed PTSD and non-trauma controls indicates that trauma survivors might show a PTSD-like

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- 1 physiological pattern while they are psychologically resilient. One could hypothesize that trauma
- 2 survivors who do not develop PTSD might be less involved in dealing with the traumatic experience,
- 3 and that this in turn might lead to long lasting symptom-like physiological patterns. Long-term
- 4 prospective studies are needed to find out more about the relationship of psychological and
- 5 physiological symptoms after traumatic experiences.

## References

- American Psychiatric Association, 1994. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. American Psychiatric Association, Washington, DC.
- Beck, A.T., Ward, C.H., Mendelson, M., Mock, J., Erbaugh, J., 1961. An inventory for measuring depression. *Archives of General Psychiatry* 4, 561-571.
- Blake, D.D., Weathers, F.W., Nagy, L.M., Kaloupek, D.G., Gusman, F.D., Charney, D.S., Keane, T.M., 1995. The development of a Clinician-Administered PTSD Scale. *Journal of Traumatic Stress* 8, 75-90.
- Blanchard, E.B., Hickling, E.J., Taylor, A.E., Loos, W.R., 1995. Psychiatric morbidity associated with motor vehicle accidents. *Journal of Nervous and Mental Disease* 183, 495-504.
- Blanchard, E.B., Hickling, E.J., Taylor, A.E., Loos, W.R., Gerardi, R.J., 1994. Psychological morbidity associated with motor vehicle accidents. *Behaviour Research and Therapy* 32, 283-290.
- Butler, R.W., Braff, D.L., Rausch, J.L., Jenkins, M.A., Sprock, J., Geyer, M.A., 1990. Physiological evidence of exaggerated startle response in a subgroup of Vietnam veterans with combat-related PTSD. *American Journal of Psychiatry* 147, 1308-1312.
- Carson, M.A., Metzger, L.J., Lasko, N.B., Paulus, L.A., Morse, A.E., Pitman, R.K., Orr, S.P., 2007. Physiologic reactivity to startling tones in female Vietnam nurse veterans with PTSD. *Journal of Traumatic Stress* 20, 657-666.
- Ehlers, A., Mayou, R.A., Bryant, B., 1998. Psychological predictors of chronic posttraumatic stress disorder after motor vehicle accidents. *Journal of Abnormal Psychology* 107, 508-519.
- Foa, E.B., 1995. PDS (Posttraumatic Stress Diagnostic Scale) Manual. Natl. Comput. Syst., Minneapolis.
- Fridlund, A.J., Cacioppo, J.T., 1986. Guidelines for human electromyographic research. *Psychophysiology* 23, 567-589.
- Grillon, C., Morgan, C.A., 3rd, Davis, M., Southwick, S.M., 1998. Effect of darkness on acoustic startle in Vietnam veterans with PTSD. *American Journal of Psychiatry* 155, 812-817.
- Guthrie, R.M., Bryant, R.A., 2005. Auditory startle response in firefighters before and after trauma exposure. *American Journal of Psychiatry* 162, 283-290.
- Hautzinger, M., Bailer, M., Worall, H., Keller, F., 1995. Beck-Depressions-Inventar (BDI). Testhandbuch (2nd ed.). Hans Huber, Bern.

## Startle reactivity in the long-term: preliminary data

- Jovanovic, T., Norrholm, S.D., Fennell, J.E., Keyes, M., Fiallos, A.M., Myers, K.M., Davis, M., Duncan, E.J., 2009. Posttraumatic stress disorder may be associated with impaired fear inhibition: relation to symptom severity. *Psychiatry Research* 167, 151-160.
- Jovanovic, T., Sakoman, A.J., Kozaric-Kovacic, D., Mestrovic, A.H., Duncan, E.J., Davis, M., Norrholm, S.D., 2012. Acute stress disorder versus chronic posttraumatic stress disorder: Inhibition of fear as a function of time since trauma. *Depression and Anxiety*.
- Koren, D., Arnon, I., Klein, E., 1999. Acute stress response and posttraumatic stress disorder in traffic accident victims: A one-year prospective, follow-up study. *American Journal of Psychiatry* 156, 367–373.
- Landis, C., Hunt, W.A., 1939. *The Startle Pattern*. Farrar & Rinehart, New York.
- Lang, P.J., Bradley, M.M., Cuthbert, B.N., 1990. Emotion, attention, and the startle reflex. *Psychology Review* 97, 377-395.
- Laux, L., Glanzmann, P., Schaffner, P., Spielberger, C.D., 1981. *Das State-Trait-Angstinventar*. Beltz, Weinheim.
- Medina, A.M., Mejia, V.Y., Schell, A.M., Dawson, M.E., Margolin, G., 2001. Startle reactivity and PTSD symptoms in a community sample of women. *Psychiatry Research* 101, 157-169.
- Metzger, L.J., Orr, S.P., Berry, N.J., Ahern, C.E., Lasko, N.B., Pitman, R.K., 1999. Physiologic reactivity to startling tones in women with posttraumatic stress disorder. *Journal of Abnormal Psychology* 108, 347-352.
- Morgan, C.A., 3rd, Grillon, C., Lubin, H., Southwick, S.M., 1997. Startle reflex abnormalities in women with sexual assault-related posttraumatic stress disorder. *American Journal of Psychiatry* 154, 1076-1080.
- Morgan, C.A., 3rd, Grillon, C., Southwick, S.M., Davis, M., Charney, D.S., 1996. Exaggerated acoustic startle reflex in Gulf War veterans with posttraumatic stress disorder. *American Journal of Psychiatry* 153, 64-68.
- Nalloor, R., Bunting, K., Vazdarjanova, A., 2011. Predicting impaired extinction of traumatic memory and elevated startle. *PLoS One* 6, e19760.
- Orr, S.P., Lasko, N.B., Metzger, L.J., Pitman, R.K., 1997a. Physiologic responses to non-startling tones in Vietnam veterans with post-traumatic stress disorder. *Psychiatry Research* 73, 103-107.

## Startle reactivity in the long-term: preliminary data

- Orr, S.P., Lasko, N.B., Shalev, A.Y., Pitman, R.K., 1995. Physiologic responses to loud tones in Vietnam veterans with posttraumatic stress disorder. *Journal of Abnormal Psychology* 104, 75-82.
- Orr, S.P., Solomon, Z., Peri, T., Pitman, R.K., Shalev, A.Y., 1997b. Physiologic responses to loud tones in Israeli veterans of the 1973 Yom Kippur War. *Biological Psychiatry* 41, 319-326.
- Pole, N., 2007. The psychophysiology of posttraumatic stress disorder: a meta-analysis. *Psychological Bulletin* 133, 725-746.
- Schnyder, U., Moergeli, H., 2002. German version of Clinician-Administered PTSD Scale. *Journal of Traumatic Stress* 15, 487-492.
- Schnyder, U., Moergeli, H., Klaghofer, R., Buddeberg, C., 2001. Incidence and prediction of posttraumatic stress disorder symptoms in severely injured accident victims. *American Journal of Psychiatry* 158, 594-599.
- Schnyder, U., Wittmann, L., Friedrich-Perez, J., Hepp, U., Moergeli, H., 2008. PTSD following accidental injury: rule or exception in Switzerland? *Psychotherapy and Psychosomatics* 77, 111-118.
- Shalev, A.Y., Orr, S.P., Peri, T., Schreiber, S., Pitman, R.K., 1992. Physiologic responses to loud tones in Israeli patients with posttraumatic stress disorder. *Archives of General Psychiatry* 49, 870-875.
- Shalev, A.Y., Peri, T., Brandes, D., Freedman, S., Orr, S.P., Pitman, R.K., 2000. Auditory startle response in trauma survivors with posttraumatic stress disorder: a prospective study. *American Journal of Psychiatry* 157, 255-261.
- Shalev, A.Y., Peri, T., Orr, S.P., Bonne, O., Pitman, R.K., 1997. Auditory startle responses in help-seeking trauma survivors. *Psychiatry Research* 69, 1-7.
- Sheehan, D.V., Lecrubier, Y., Sheehan, K.H., Amorim, P., Janavs, J., Weiller, E., Hergueta, T., Baker, R., Dunbar, G.C., 1998. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *Journal of Clinical Psychiatry* 59 (Suppl 20), 22-33;quiz 34-57.
- Ursano, R.J., Fullerton, C.S., Epstein, R.S., Crowley, B., Kao, T.C., Vance, K., Craig, K.J., Dougall, A.L., Baum, A., 1999. Acute and chronic posttraumatic stress disorder in motor vehicle accident victims. *American Journal of Psychiatry* 156, 589-595.

# Startle reactivity in the long-term: preliminary data

Table 1

Sample description.

|                             | PTSD-remitted |             | Trauma controls |             | Non-trauma controls |             |                        |             |          |
|-----------------------------|---------------|-------------|-----------------|-------------|---------------------|-------------|------------------------|-------------|----------|
|                             | <i>N</i>      | %           | <i>N</i>        | %           | <i>N</i>            | %           | <i>Chi<sup>2</sup></i> | <i>d.f.</i> | <i>P</i> |
| Men                         | 5             | 38.5        | 5               | 41.7        | 6                   | 37.5        | 0.05                   | 2           | 0.9      |
| Women                       | 8             | 61.5        | 7               | 58.3        | 10                  | 62.5        |                        |             |          |
|                             | <i>M</i>      | <i>S.D.</i> | <i>M</i>        | <i>S.D.</i> | <i>M</i>            | <i>S.D.</i> | <i>F</i>               | <i>d.f.</i> | <i>P</i> |
| Age                         | 53.2          | 9.3         | 58.5            | 7.2         | 54.1                | 10.3        | 1.22                   | 2/38        | 0.3      |
| Years of education          | 13.5          | 2.9         | 13.8            | 2.3         | 15.1                | 3.9         | 1.09                   | 2/38        | 0.3      |
| STAI - trait anxiety        | 34.46         | 4.31        | 32.42           | 4.17        | 35.5                | 6.6         | 1.17                   | 2/38        | 0.3      |
| BDI - depression            | 7.54          | 3.38        | 6.17            | 3.97        | 5.19                | 4.49        | 1.23                   | 2/38        | 0.3      |
|                             | <i>M</i>      | <i>S.D.</i> | <i>M</i>        | <i>S.D.</i> | <i>M</i>            | <i>S.D.</i> | <i>t</i>               | <i>d.f.</i> | <i>P</i> |
| CAPS – current total score  | 6.5*          | 8.22*       | 2.58            | 4.17        |                     |             | -1.47                  | 22          | 0.2      |
| Years since trauma exposure | 11.5          | 1.8         | 9.9             | 0.3         |                     |             | 3.3                    | 12.9        | 0.006    |
| Years without symptoms      | 7.3           | 5.2         |                 |             |                     |             |                        |             |          |

Note: STAI= State Trait Anxiety Inventory, BDI= Beck Depression Inventory, CAPS= Clinician-Administered PTSD Scale. \* Missing CAPS data in one subject.



### Startle reactivity in the long-term: preliminary data

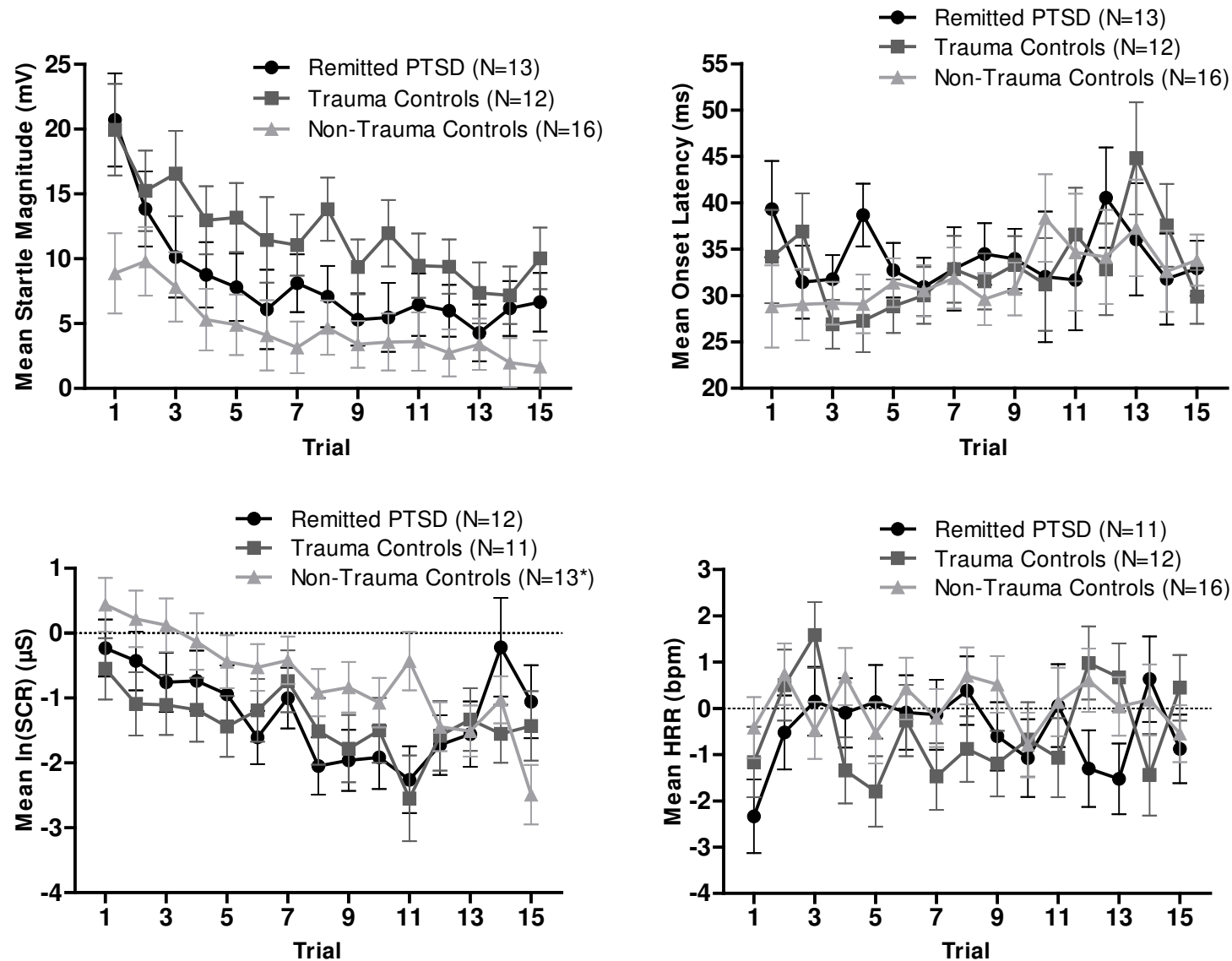


Figure 1. Estimated marginal means and standard errors for the time course of eye-blink magnitude in millivolt (top left), eye-blink onset latency in milliseconds (top right), natural logarithm of skin conductance response in micro Siemens (bottom left) and heart rate response in beats per minute (bottom right). \* One of 14 subjects dropped out of skin conductance analysis because none of the responses reached the threshold of 0.05  $\mu$ S

## **Startle reactivity in the long-term after severe accidental injury:**

### **Preliminary data**

Sonja Schumacher, Ulrich Schnyder, Michael Furrer, Christoph Mueller-Pfeiffer, Frank H. Wilhelm, Hanspeter Moergeli, Misari Oe, Chantal Martin-Soelch

### **Supplemental material**

This material supplements but does not replace the content of the peer-reviewed paper published in Psychiatry Research.

### **Results without subjects taking psychotropic medication**

There was a significant main effect of group on eye-blink magnitude ( $F(2, 52.8)=3.62, P=0.03$ ). The trauma-controls showed significantly higher eye-blink magnitude ( $M=11.90, SE=2.06$ ) than the non-trauma controls ( $M=4.61, SE=1.77$ ) (mean difference=7.30,  $SE=2.72$ , 95%-CI 0.58 to 14.01,  $P=0.03$ ). There was neither a significant difference in eye-blink magnitude between remitted PTSD subjects ( $M=7.35, SE=2.14$ ) and the trauma-controls (mean difference=-4.55,  $SE=2.97$ , 95%-CI -11.89 to 2.80,  $P=0.4$ ) nor between the remitted PTSD subjects and the non-trauma controls (mean difference=2.75,  $SE=2.78$ , 95%-CI -4.13 to 9.62,  $P=1.0$ ). There was a significant main effect of time on eye-blink magnitude ( $F(14, 54.6)=3.99, P<0.001$ ) with magnitude decreasing over time across all groups of subjects. Skin conductance response showed a significant main effect of time ( $F(14, 89.8)=6.83, P<0.001$ ), decreasing over time across all groups of subjects. There was no significant main effect of group for skin conductance response ( $P=0.4$ ). No significant main effects were found for eye-blink onset latency and heart rate response ( $P_s>0.07$ ). No significant time by group interaction was found in any of the measures ( $P_s>0.1$ ).

### **Separate model for trials 1 to 6 (all subjects)**

There was no significant main effect of group on eye-blink magnitude ( $P=0.1$ ). There was a significant main effect of time on eye-blink magnitude ( $F(5, 49.0)=6.83, P<0.001$ ) with magnitude decreasing over time across all groups of subjects. Skin conductance response showed a significant main effect of time ( $F(5, 68.5)=6.22, P<0.001$ ), decreasing over time across all groups of subjects. There was no significant main effect of group for skin conductance response ( $P=0.1$ ). No significant

## Startle reactivity in the long-term: preliminary data

main effects were found for eye-blink onset latency and heart rate response ( $P_s \geq 0.06$ ). No significant time by group interaction was found in any of the measures ( $P_s > 0.08$ ).

### Separate model for trials 7 to 15 (all subjects)

There was a significant main effect of group on eye-blink magnitude ( $F(2, 39.2) = 3.33$ ,  $P = 0.05$ ). The trauma-controls showed significantly higher eye-blink magnitude ( $M = 9.90$ ,  $SE = 1.99$ ) than the non-trauma controls ( $M = 3.12$ ,  $SE = 1.71$ ) (mean difference = 6.77,  $SE = 2.63$ , 95%-CI 0.21 to 13.34,  $P = 0.04$ ). There was neither a significant difference in eye-blink magnitude between remitted PTSD subjects ( $M = 6.09$ ,  $SE = 1.90$ ) and the trauma-controls (mean difference = -3.80,  $SE = 2.75$ , 95%-CI -10.69 to 3.08,  $P = 0.5$ ) nor between the remitted PTSD subjects and the non-trauma controls (mean difference = 2.97,  $SE = 2.56$ , 95%-CI -3.42 to 9.36,  $P = 0.8$ ). There was a significant main effect of time on eye-blink magnitude ( $F(8, 50.1) = 2.75$ ,  $P = 0.01$ ) with magnitude decreasing over time across all groups of subjects. Skin conductance response showed a significant main effect of time ( $F(8, 103.6) = 2.16$ ,  $P = 0.04$ ), decreasing over time across all groups of subjects. There was no significant main effect of group for skin conductance response ( $P = 0.9$ ). No significant main effects were found for eye-blink onset latency and heart rate response ( $P_s > 0.2$ ). No significant time by group interaction was found in any of the measures ( $P_s > 0.2$ ).